Figure 1

A. ctc aac cag tcc att gtc ca

B. tcc cgg ttg ctc tga gac at

C. gcc aca gtc atg ccc gtc ag

D. ctg cga tcc gac tca cca at

E. agt cct gtt ctc ttc cac

F. ctt tac tgc tgc cat ggg

G. cgc cgt tct cct gga tcc aa

H. ctg act cca gct gta tcc

I. ggt ctc cat ctc cga ttc

J. cct ggg gtg atg tgg agc

K. agt tcc aca aaa gta tcc

L. ctt tcg gct ctc ggc tgc

M. aac cag cgg ttg aag cgt

Figure 2A

A. (T31028)
c*t*c* aac* cag t*c*c at*t gt*c* c*a

A'. (T31029)
C*T*C* aaC* Cag T*C*C aT*T gT*C* C*a

B. (T31030)
t*c*c* cgg t*tg c*t*c* tga ga*c* a*t

C. (T31044)
g*c*c* aca gt*c atg c*c*c gt*c* a*g

C'. (T31045)
g*C*C* aCa gT*C aTg C*C*C gT*C* a*g

D. (T31049)
CT*g Cga T*C*C gaC* T*Ca C*C*a* a*t

E. (T31054)
a*g*t* c*c*t gt*t c*t*c t*t*c* c*a*c

E'. (T31055)
a*g*T* C*C*C* g*T*T C*T*C T*T*C* C*a*c

F. (T31061)
C*T*T* TaC TgC* TgC* CaT* g*g*g

G. (T31043)
C*gC* C*gT* T*C*T* C*C*T gga TC*C* a*a

G'. (T31042)
c*gc* c*gt* t*c*t* c*c*t gga tc*c* a*

Figure 2B

H. (T31053)
C*T*g* aC*T* C*Ca gC*T gTa* T*C*c

H'. (T31052)
c*t*g* ac*t* c*ca gc*t gta* t*c*c

I. (T31057)
g*g*T* CT*C* CaT* CT*C Cga* T*T*c

I'. (T31056)
g*g*t* ct*c* cat* ct*c cga* t*t*c

J. (T31062/63)
c*c*t* ggg gtg* atg* tgg* a*g*c

K. (T31065)
a*g*T* TC*C aC*a aaa gT*a* T*C*c

K'. (T31064)
a*g*t* tc*c ac*a aaa gt*a* t*c*c

L. (T31067)
C*T*T* Tcg gC*T C*T*C ggC* T*g*c

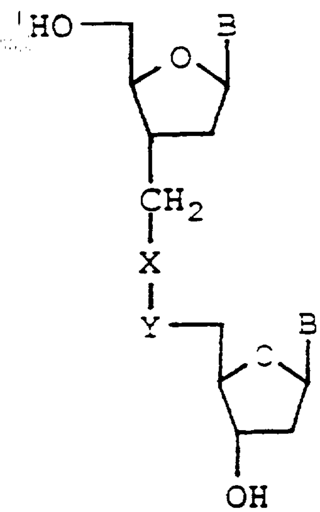
L' (T31066)
c*t*t* tcg gc*t c*t*c ggc* t*g*c

M. (T31069)
a*a*C* Cag Cgg T*Tg aag* C*g*t

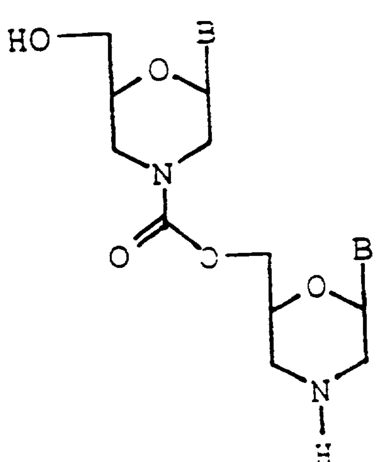
M'. (T31068)
a*a*c* cag cgg t*t*g aag* c*g*t

where * = phosphorothioate
C = Propynyl dC
T = Propynyl dT

Figure 3A

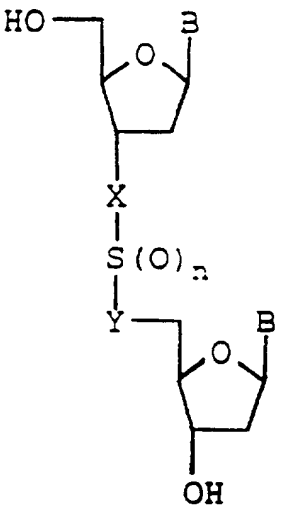


	X	Y
Hydroxylamine	N-H	O
MOMI	O	$N-CH_3$
MMI	$N-CH_3$	O

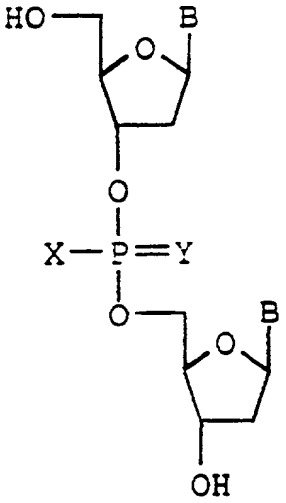


Morpholino-carbamate

Figure 3B

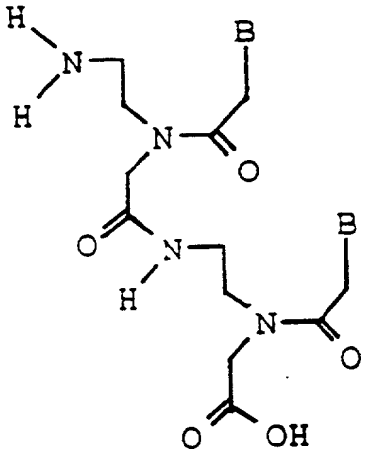


	X	Y
n = 2		
Sulfate	O	O
Sulfonate	O	CH_2
Sulfone	CH_2	CH_2
Sulfamate	O	NH
Sulfonamide	NH	CH_2
n = 1		
Sulfite	O	O
Sulfoxide	CH_2	CH_2
n = 0		
Sulfide	CH_2	CH_2

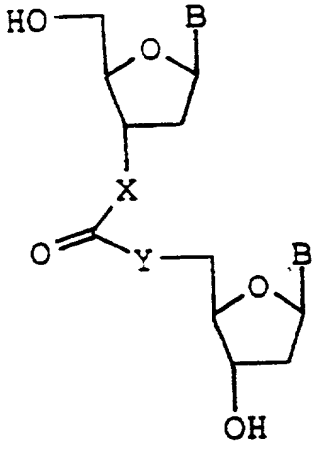


	X	Y
Phosphodiester	O^-	O
Phosphorothioate	S^-	O
Phosphorodithioate	S^-	S
Methylphosphonate	CH_3	O
Phospnotriester	O-R	O
Phosphoramidate	NH-R	O
Boranophosphate	BH_3	O

Figure 3C



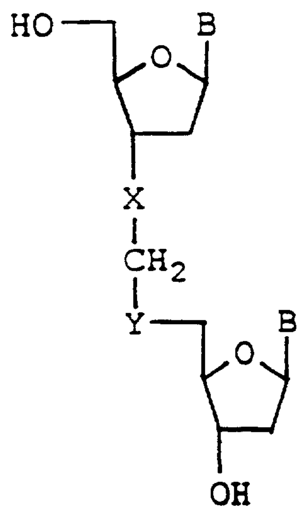
PNA dimer



Carbonate

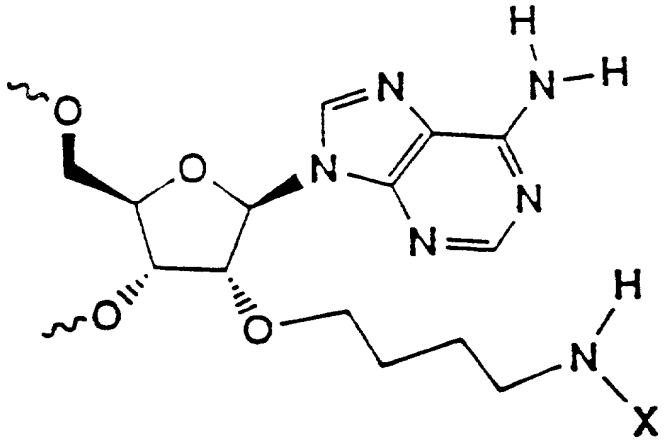
5'-N-carbamate

Figure 3D



	X	Y
Formacetal	O	O
5'-Thioether	CH_2	S
3'-Thioformacetal	S	O
5'-Thioformacetal	O	S

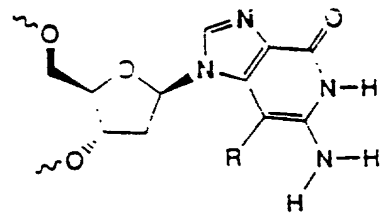
Figure 4



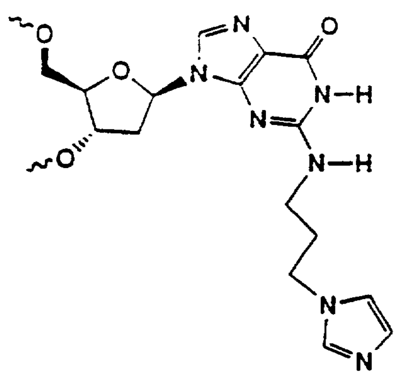
X = BIOTIN
= CHOLIC ACID
= FLUORESCEIN

2'-O-(AMINOPENTYL) ADENINE CONJUGATES

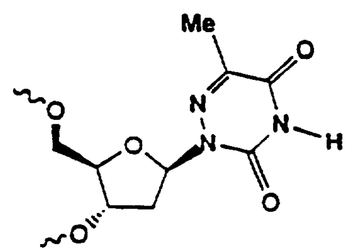
Figure 5A



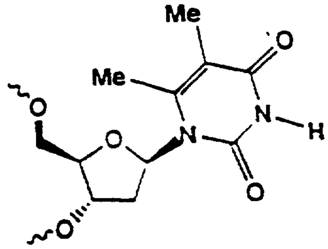
3-DEAZAGUANINES



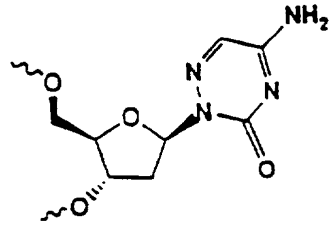
N2-IMIDAZOLYLPROPYL
GUANINE



6-AZATHYMIDINE

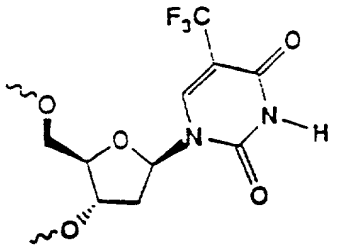


5,6-DIMETHYLTHYMIDINE

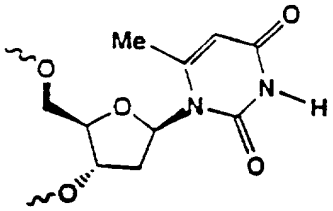


6-AZA-DEOXYCYTIDINE

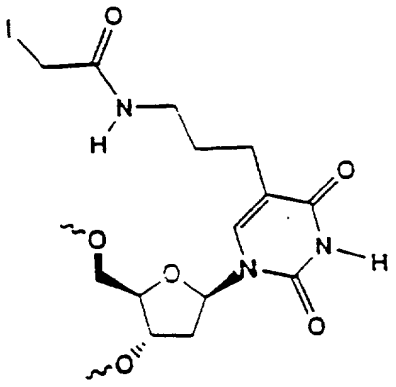
Figure 5B



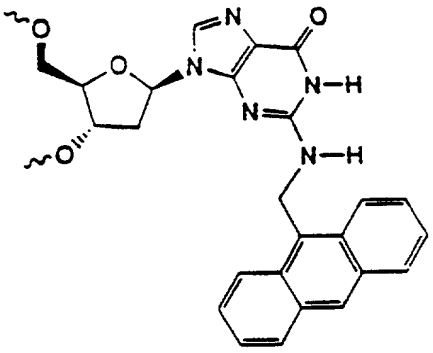
TRIFLUOROTHYMINE



6-METHYLTHYMIDINE



IODOACETAMIDOPROPYL URACIL



N2-ANTRACENYLMETHYL GUANINE

FIGURE 6 Effect of 18-mer PS oligonucleotides on bcl-xL protein expression in LNCaP cells

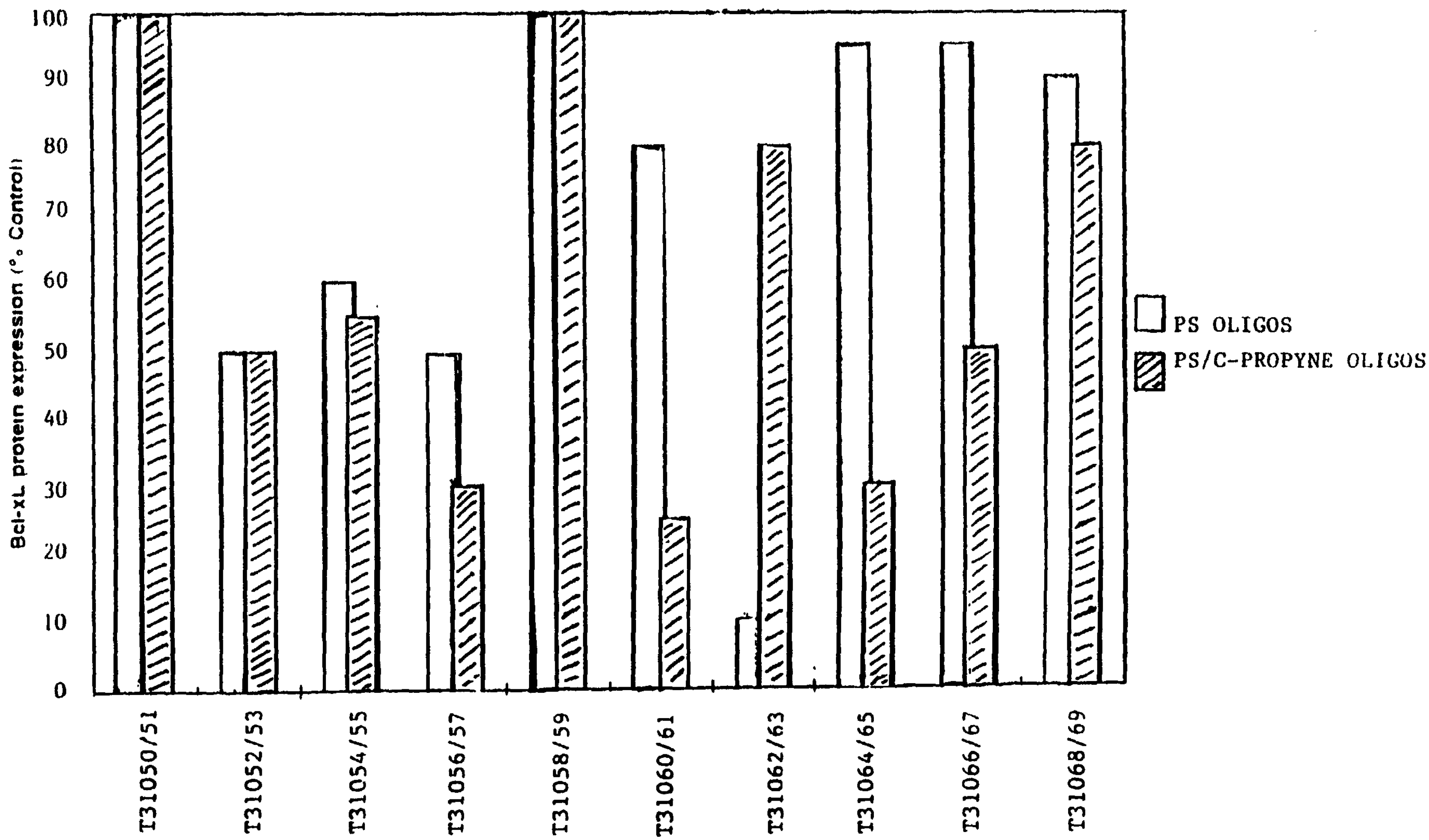
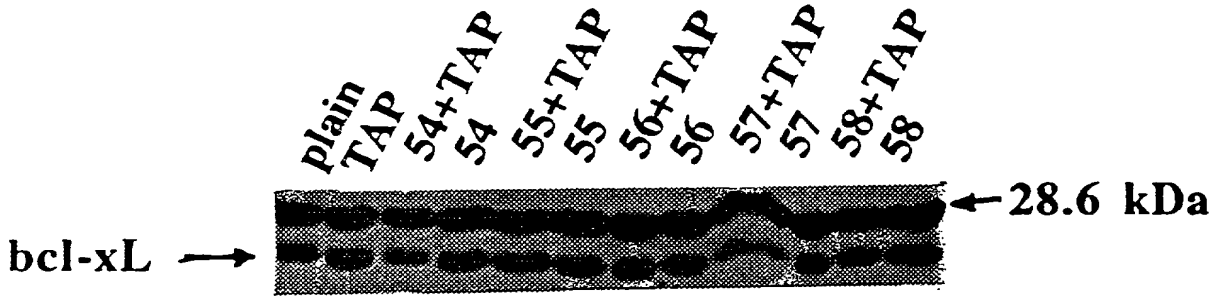


FIGURE 7

LNCaP cell line



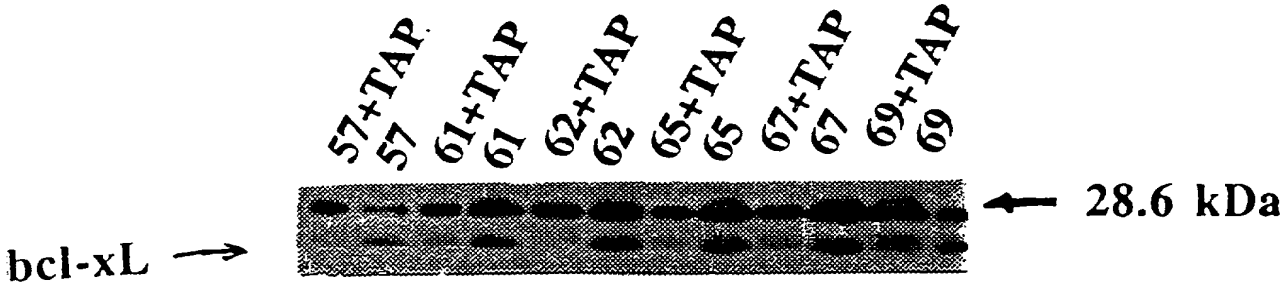


FIG. 8

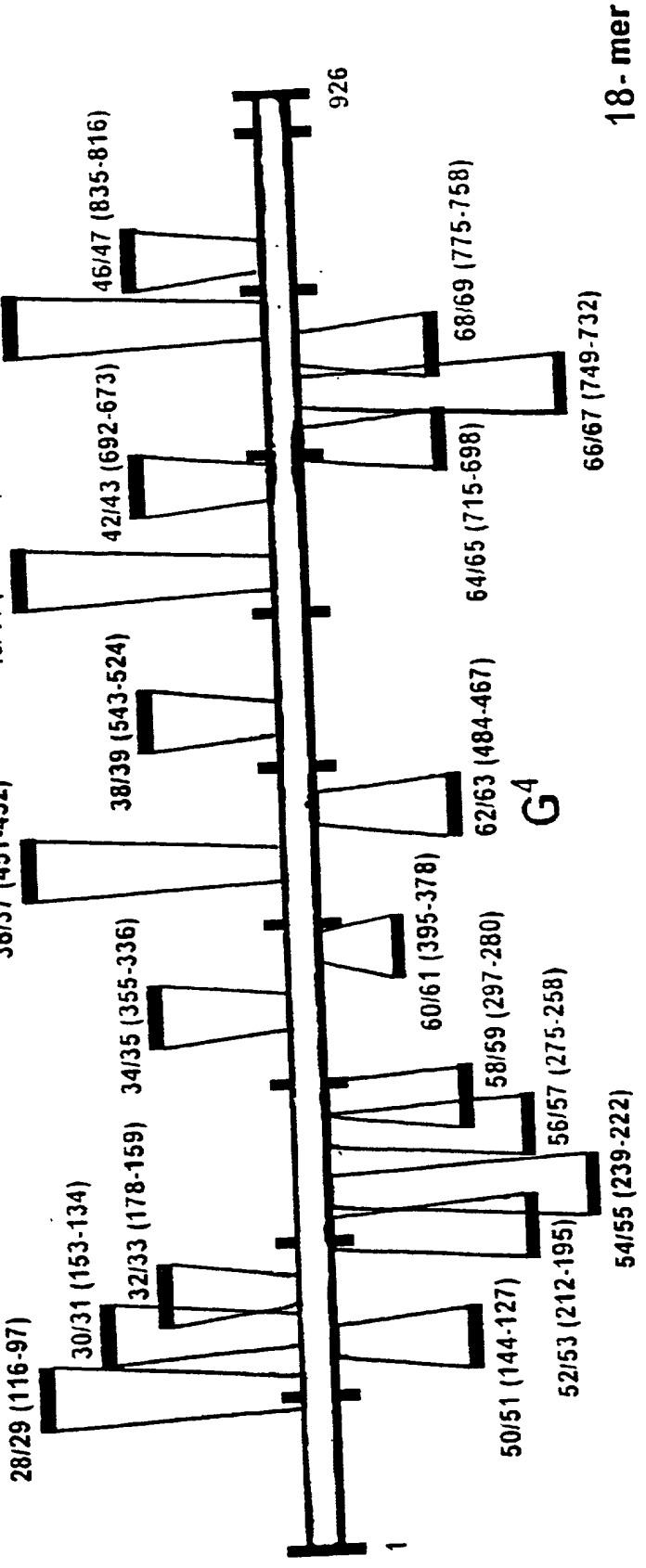
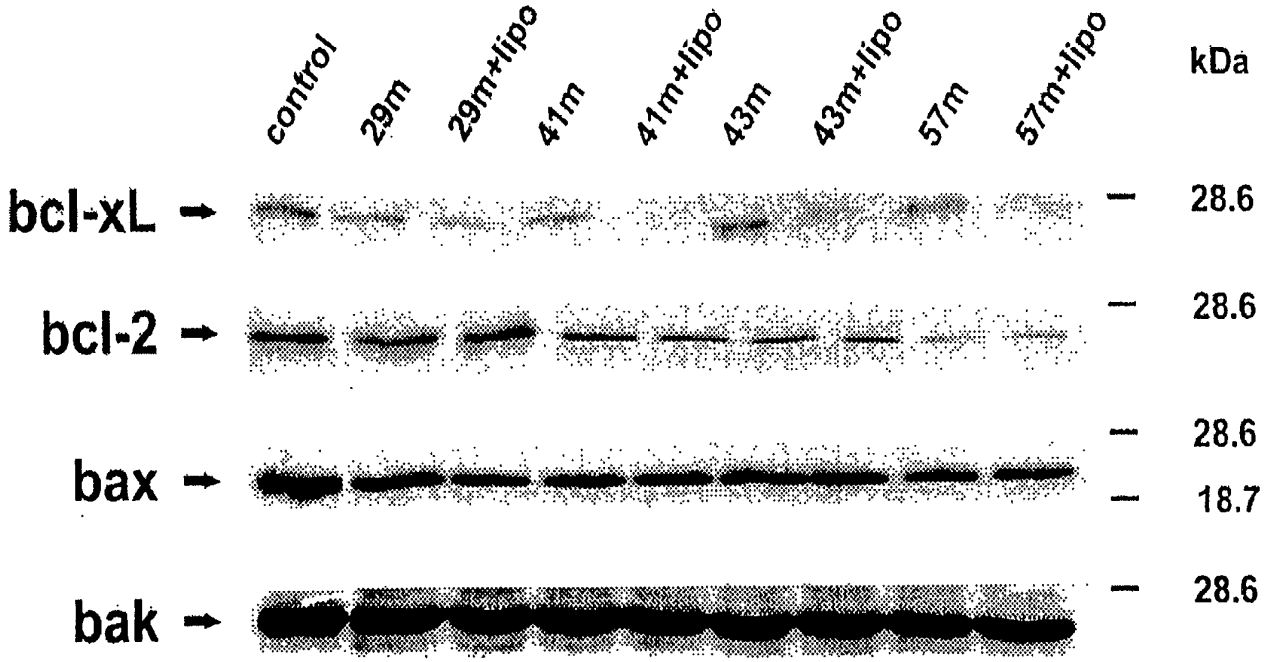

Antisense Oligonucleotides to Bcl-xL mRNA
20-mer
18-mer
1
926
28/29 (116-97)
30/31 (153-134)
32/33 (178-159)
34/35 (355-336)
36/37 (451-432)
38/39 (543-524)
40/41 (635-616)
42/43 (692-673)
44/45 (795-776)
46/47 (835-816)
50/51 (144-127)
52/53 (212-195)
54/55 (239-222)
56/57 (275-258)
58/59 (297-280)
60/61 (395-378)
62/63 (484-467)
64/65 (715-698)
66/67 (749-732)
68/69 (775-758)
G4

FIG. 9

Regulation of Bcl-Family Proteins with 2'-O-Methyl - Modified PS Oligonucleotides in T24 Cell Line



Delivery: 1 uM oligo, 5 ug/ml Lipofectin

FIG. 10

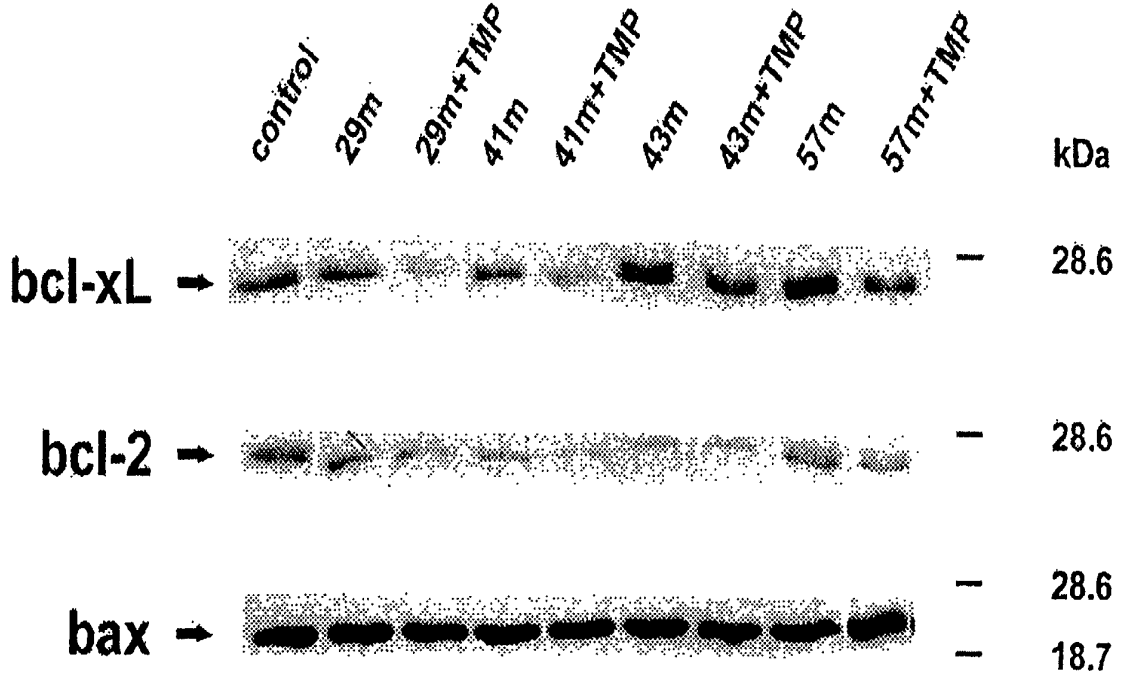
The Most Acitve Chimeric PS-PO Oligonucleotides by
Their Ability to Down-Regulate Bcl-xL Protein Expression

#	5'-	-3'
29	C*T*C* a a C* C a g T*C*C a T*T g T*C* C*a	
41	C T*g* C g a T*C*C g a C* T*C a C*C*a* a*t	
43	C*g C* C*g T* T*C*T* C*C*T g g a T C *C* a*a	
57	g*g*T* C T C* C a T* C T*C C g a* T*T*c	
61	C*T*T* T a C T g C* T g C* C a T* g*g*g*	
62	c*c*t* g g g g t g* a t g* t g g* a*g*c	
63	C*C*T* g g g g T g* a T g* t g g* a*g*	

C, T - propynyl modified bases, * - PS

FIG. 11

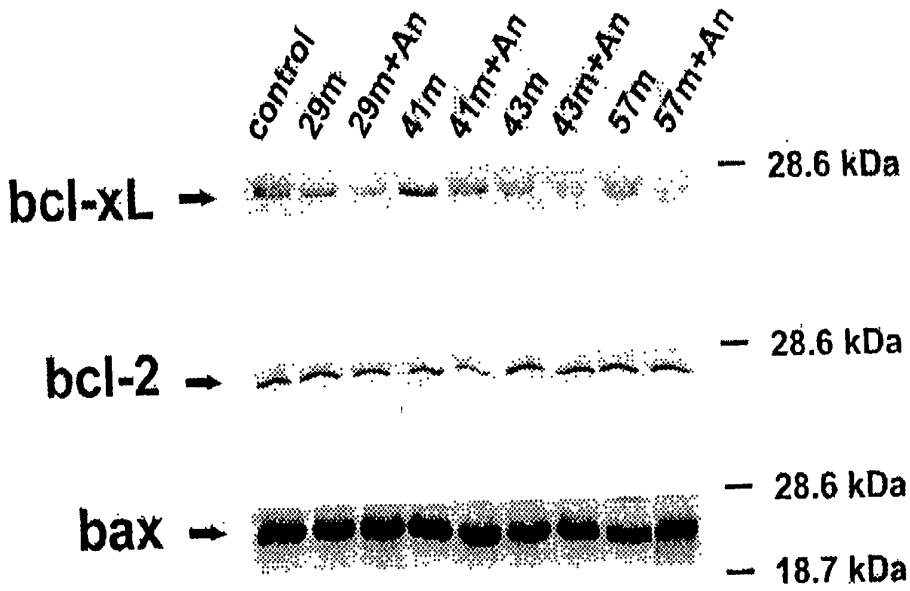
Regulation of Bcl-Family Proteins with 2'-O-Methyl - Modified PS Oligonucleotides in PC - 3 Cell Line



Delivery: 1uM oligo, 5 uM TMP

FIG. 12

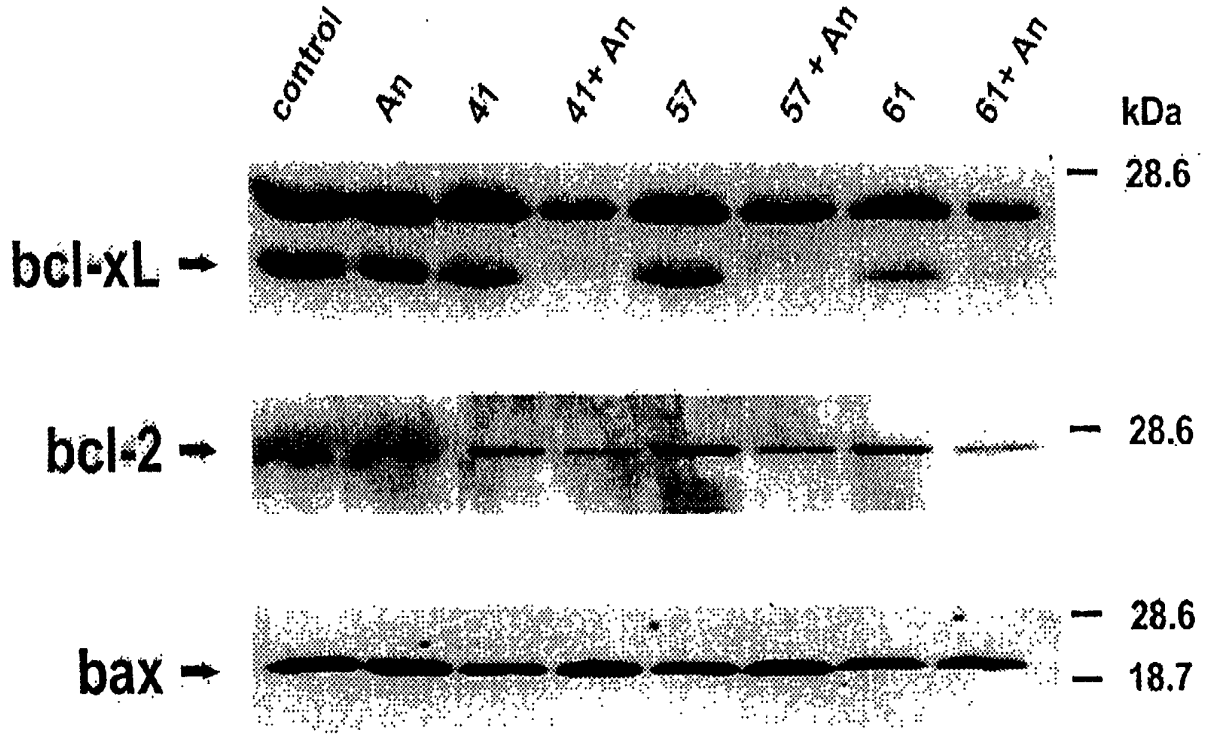
Regulation of Bcl-xL and Bax Proteins with 2'-O-Methyl-Modified PS Oligonucleotides in LNCaP Cell Line



Delivery: 1 uM oligo, 5 uM An

FIG. 13

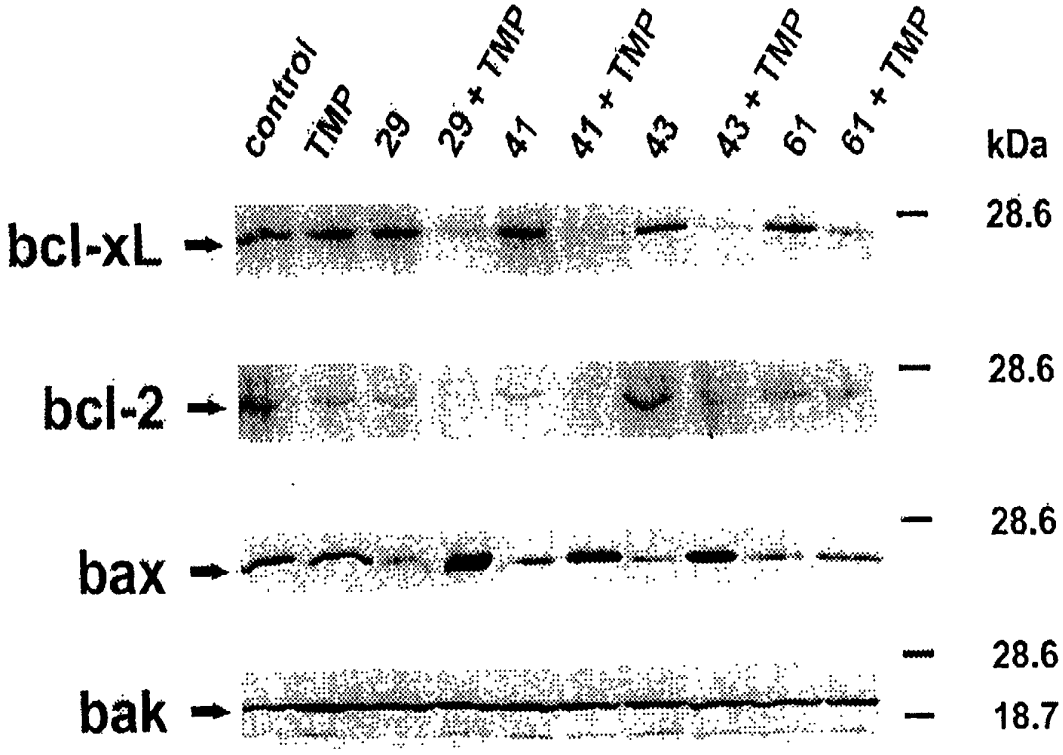
Down-Regulation of Bcl-Family Proteins Expression with PS-PO Oligonucleotides in LNCaP Cell Line



Delivery: 1uM oligo, 3 uM An

FIG. 14

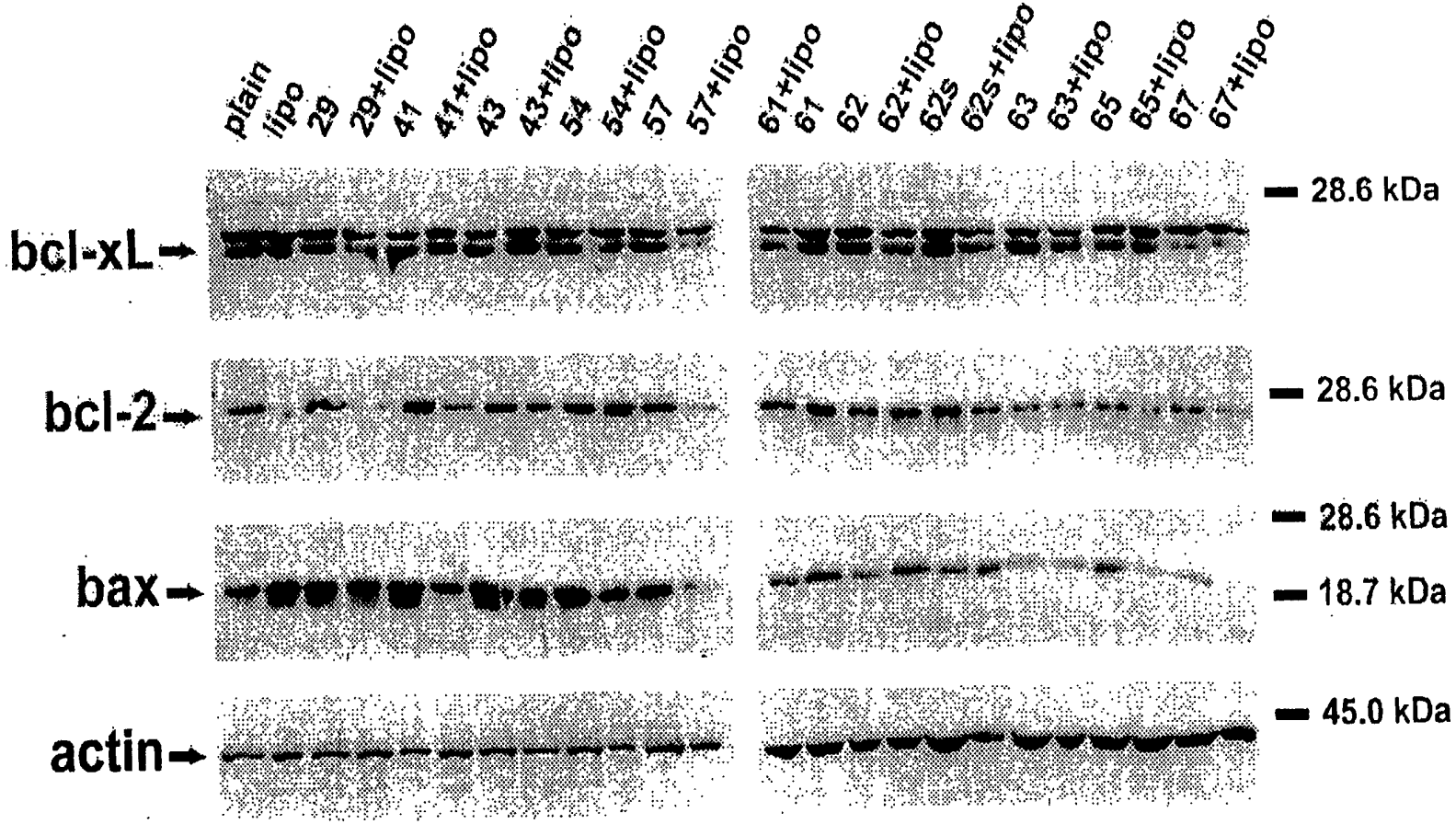
Down-Regulation of Bcl-Family Proteins Expression with PS-PO Oligonucleotides in PC3 Cell Line



Delivery: 2 uM oligo, 7 uM TMP

FIG. 15

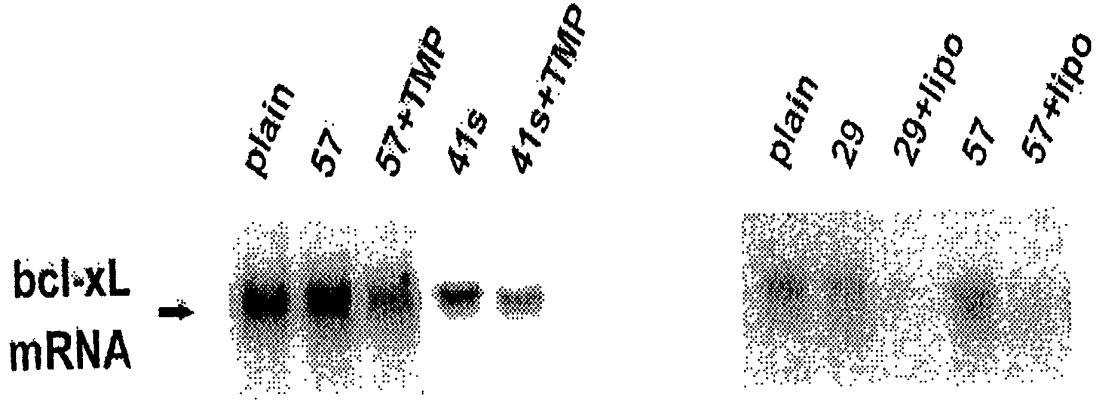
Regulation of Bcl-Family Proteins with PS-PO Oligonucleotides in T24 Cell Line



Delivery: 0.5 uM oligo, 5 mg/ml lipofectin

FIG. 16

Down-Regulation of Bcl-xL mRNA with PS-PO Oligonucleotides in T24 Cell Line

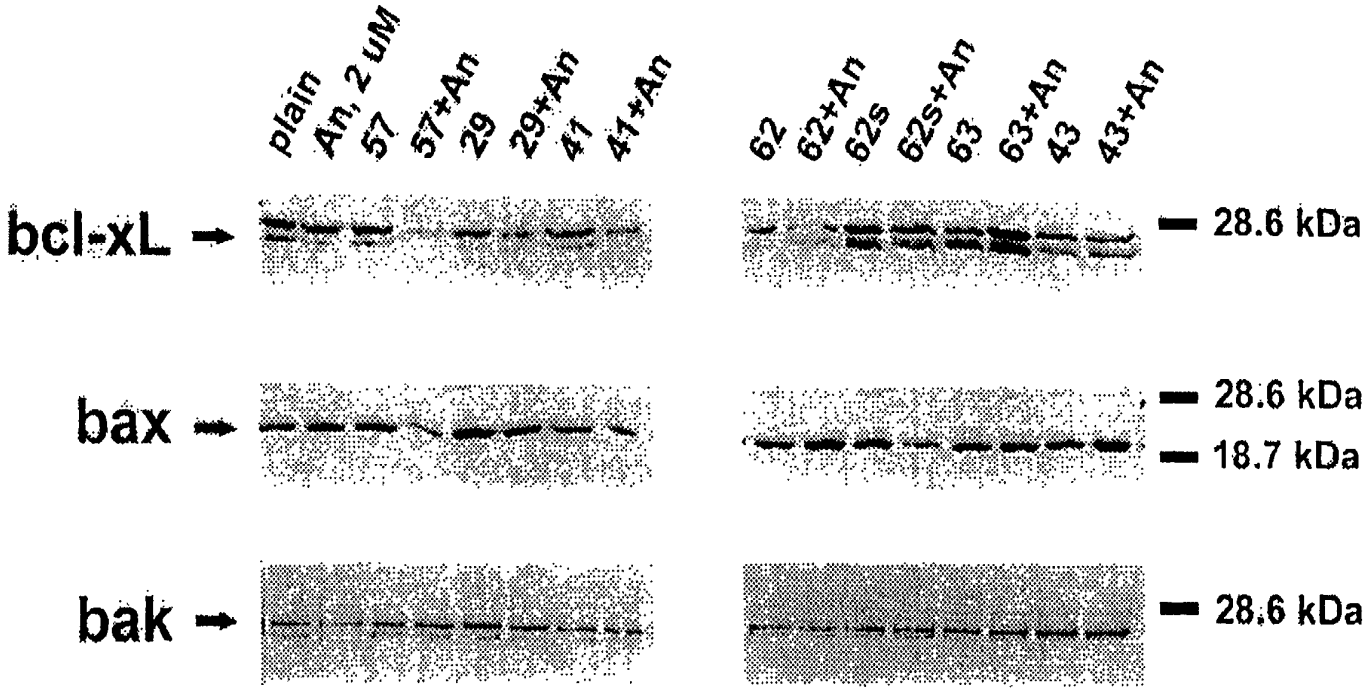


Delivery: 9 uM TMP, 3 uM oligo

5 ug/ml lipofectin 1 uM oligo

FIG. 17

Regulation of Bcl-Family Proteins with PS-PO Oligonucleotides in LNCaP Cell Line



Delivery: 1 uM oligo, 3 uM An